patients have elevated urine calcium during both high and low calcium intake. Serum calcium and PTH are normal. Thiazide diuretics or cellulose phosphate are effective treatments and decrease urinary calcium excretion. Type II hypercalciurics exhibit hypercalciuria only during increased calcium dietary intake. Therapy is directed at decreasing dietary calcium by about 50% to approximately 400 mg/day; over the long term bone density is stable. Type III absorptive hypercalciuria is secondary to a renal phosphate "leak". The low serum phosphate stimulates vitamin D and subsequent absorption of phosphate and calcium. Treatment with bioavailable phosphate (neutral orthophosphate) is effective.

Resorptive hypercalciuria is due to primary hyperparathyroidism and is treated with surgical removal of the parathyroid adenoma.

Renal "leak" hypercalciuria is caused by defective tubular reabsorption of calcium. Secondary hyperparathyroidism is often noted. This condition is successfully treated over the long term with thiazides.

Hyperuricosuria, hypocitraturia and hyperoxaluria comprise the normocalciuric conditions associated with calcium lithiasis. Hyperuricosuria may be associated with gout, myeloproliferative states and malignancy but is most frequently due to dietary overindulgence. Monosodium urate crystals act as nidi for calcium oxalate stones by heterogeneous nucleation. Decreased sodium intake is critical for management, as with hypercalciuric states. If reduced intake of dietary purines is unsuccessful, allopurinol is usually effective.

Hyperoxaluria is most commonly due to chronic diarrheal states such as inflammatory bowel disease. Increased fecal fats bind to intraluminal calcium, thus calcium is unavailable to bind to oxalate which is readily absorbed. Mild cases may be controlled with intake of calcium rich foods with meals to bind dietary oxalates. More severe cases may require calcium containing antacids at mealtime.

Citrate is a potent inhibitor of calcium lithiasis, acting by complexing with urinary calcium in solution. Low urinary citrate (<320 mg/day) is associated with conditions resulting in a metabolic acidosis (i.e., chronic thiazide use, renal tubular acidosis, diarrhea). These patients are successfully treated with citrate supplements, such as potassium citrate or naturally occurring citrate found in lemonade.

The three most common non-calcium stones are uric acid, struvite, and cystine. Less common stones may be matrix, xanthine, or drug related (triamterene and indinavir).

Uric acid calculi are relatively radiolucent and patients consistently have urinary pH <5.5. The stones may be dissolved with urinary alkalinization (oral KCitrate or K bicarbonate) at a rate of 0.5 cm per month. Solubility of uric acid rapidly rises above pH 6.0. As with all stone formers, patients should be encouraged to maintain a urinary output of 1.5-2.0 liters per day. They are encouraged to drink fluid with meals, 2 hours after each meal, and prior to bedtime, adequate enough to awaken the patient to void.

Struvite stones (magnesium ammonium phosphate) occur in the presence of infection with urea-splitting organisms and are most commonly seen in women. They frequently present with non- E. coli recurrent urinary tract infections. Sterilization of the calculi using antibiotics is futile; surgical removal of the infected stones remains the cornerstone of treatment. A full metabolic evaluation is necessary because most stones are of mixed composition and metabolic defects may be identified.

Cystinuria is a hereditary defect affecting the transport of dibasic amino acids in the small bowel and renal tubules. Elevated levels of urinary cystine precipitate at normal urinary pH (5.8-6.0); the solubility of cystine increases above pH 7.5. Treatment centers on urinary alkalization, hydration and sulfhydryl binding agents such as alpha mercaptopropionyl glycine (Thiola).

Urinary stone disease is common and is usually characterized by acute onset of severe colic. Stone size does not correlate with the severity of symptoms. Frequently, small ureteral stones are most painful. Although recurrences often mark the course of this disease, dietary manipulation and medical therapies can result in stone prevention and avoidance of complications.

NOAH S. SCHENKMAN, MD
MARSHALL L. STOLLER, MD
San Francisco, California

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Epidemiology of Prostate Cancer

IN 1996 ALONE, 317,000 men were diagnosed with carcinoma of the prostate. The overall incidence.showed a slight rise in 1989 followed by a sharp rise in 1991, peaking in 1992–93. Since then, there has been a gradual decline. The observed increase is a response to an aggressive nationwide prostate screening program.

It has long been known that the incidence of prostate cancer increases with age. Of major significance and interest now are the varying rates of incidence of prostate cancer according to racial distribution. The incidence is highest among African-Americans at 188 per 100,000 person-years, intermediate among whites at 139 per 100,000 person-years and lowest among Asians at 39 per 100,000 person-years for Japanese and 28 per 100,000 person-years for Chinese. Of significance is the observation that Asians living in the United States have a higher incidence of prostate cancer than those residing in their country of origin, but still lower than whites and African-Americans.

In addition to a higher incidence, it appears that African-American men with prostate cancer have a higher grade and larger cancer volume when compared to Caucasian men. They may also have a significantly higher prostate specific antigen (PSA) level after radical prostatectomy, suggesting a greater residual tumor bur-

den. Some feel that these data argue for aggressive and early detection programs among African-American men, although the outcome of treatment is still being evaluated.

Family history of prostate cancer is now a recognized risk factor for prostate cancer.The relative risk for a man developing it depends on the number of affected relatives (about 1.4 with one affected first degree relative and over 3 with more than one.) Current data suggest that familial prostate cancer may be a more aggressive type of cancer. Patients with familial prostate cancer have a worse outcome after radical prostatectomy than patients with nonfamilial prostate cancer. The poor result is primarily related to a higher distant relapse rate, suggesting that familial cancer is biologically more aggressive. Recent reports confirm the existence of a rare autosomal dominant prostate cancer susceptibility gene dubbed "HPC1" for "hereditary prostate cancer 1." Some feel these data argue for aggressive early screening for men with family history of prostate cancer, although outcome studies have not been completed.

In addition to the racial and familial risk factors associated with prostate cancer, several other risk factors are being hotly pursued, but are not established. Factors being evaluated include cigarette smoking and.consumption of dietary fat, tomatoes, and supplemental selenium. Other areas of interest include association with farming and history of vasectomy.

As cigarette smoking is implicated with lung cancer, it is also being investigated for its relationship with prostate cancer. Higher death rates from prostate cancer in current cigarette smokers suggesting that smoking may adversely affect survival in prostate cancer patients, however.

Dietary factors have been correlated with prostate cancer. Early studies support the hypothesis that high dietary fat intake is correlated with prostate cancer. Dietary fat intake was observed primarily with animal fat and meat consumption rather than vegetable fat consumption. Recent reports, however, tend to refute the previously asserted association, finding no link between dietary fat, especially animal sources, with risk or mortality of prostate cancer. Epidemiologic studies suggest high consumption of tomatoes or supplemental selenium may protect against prostate cancer. These findings need confirmation before dietary changes are made.

Recent reports indicate a positive correlation between prostate cancer and farming. Authors are speculate that hormonally active agricultural chemicals are potential risk factors among farmers.

The suggestion that vasectomy may increase the risk of prostate cancer is being disputed by evaluating confounding factors. For example, the odds ratio estimate for prostate cancer associated with vasectomy tended to increase among men with such known risk factors as father and brother with prostate cancer. Any increased risk may be related to detection bias or differential participation rates due to both vasectomy status and a family history of prostate cancer.

ANANIAS C. DIOKNO, MD
Royal Oak, Michigan

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Sildenafil: A Milestone in the Treatment of Impotence

WITH AN ESTIMATED 18–30 million American men who experience some degree of erectile dysfunction, it is not surprising that sildenafil, the first effective oral treament agent, released under the trade name Viagra by Pfizer Co. in April 1998, has been the fastest selling drug in pharmaceutical history. Sildenafil is an inhibitor of phosphodiesterase type 5 (PDE5). When initially investigated in patients with cardiac disease to promote vasodilatation, many reported improved erectile response.

Erections occur through sexual stimulation of the parasympathetic nervous system leading to release of the neurotransmitter nitric oxide, a powerful vasodilator derived from the endothelial cells lining the penile spaces—the corpus cavernosum. Nitric oxide then produces cyclic GMP which causes the smooth muscle of the corpus cavernosum to relax and fill with arterial blood, creating the erection. Pressure from these expanding spaces occludes veins against the tunica albugenia, surrounding the erectile tissue and leading to sustained erection.

Sildenafil works by blocking the enzyme, phosphodiesterase 5, which breaks down cyclic GMP, leading to higher sustained levels of cyclic GMP and relaxation of the smooth muscle spaces of the penis, and thereby amplifies sexual stimulation. Sildenafil has no direct effect on increasing libido but may enhance the sexual experience by decreasing performance anxiety caused by anticipated failure.

Available in 25, 50, and 100 milligram tablets,(a 50 mg tablet is the most common dose), sildenafil is taken about one hour prior to sexual activity to allow for absorption. Effects last 3–5 hours. About 70% of men with erectile dysfunction experience improved erections. Most side effects are attributable to vasodilatation: headache and flushing(10%). Additionally, about 3% of patients experience mild and transient visual effects—predominantly color tinge, but also light sensitivity—a pharmacological response thought to be related to sildenafil's weak inhibition of PDE6, found in the retina. The most serious side effect is hypotension, which may be amplified by concomitant use of nitrates, therefore, use with nitroglycerin or other nitrates is contradicted. Deaths reported to date in patients taking sildenafil do not appear to be greater than the same cohort